



***MITO 101 – Infections ( recurrent)***

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- Mitochondria are involved in multiple cell functions, including cell proliferation, differentiation and defense. Mitochondria provide essential defensive energy for leukocyte movement, bacterial ingestion and bacterial killing <sup>1</sup>.
- The leukocytes, which include lymphocytes, neutrophils, basophils and eosinophils, are key components of the immune system. In particular, the leukocytes known as T and B cells, are representative members of the adaptive immune system. The adaptive immune system is responsible for higher level immune functioning in the eradication of complex organisms <sup>2</sup>.
- T cells and B cells migrate slowly towards each other in the lymph nodes, where bacterial antigens are presented. Antigen presentation then induces B cells to produce immunoglobulins that specifically protect the respiratory system, including ears, middle ear structures, sinuses, and lungs. Without this *painfully slow mitochondrial powered waltz* of T and B cells, antigen presentation may be diminished or absent. Defects of the mitochondrial respiratory chain may impair the antigen presenting process at this nodal area. This would then predispose mitochondrial patients to recurrent respiratory tract infections, either upper or lower in nature.
  - In our studies, we have found many patients with mitochondrial defects suffer from recurrent upper or lower respiratory tract infections, and demonstrate poor antibody response to polysaccharide antigens. These recurrent infections contribute to the ultimate deterioration of the patient. It is clear that elimination of the infections would slow down the progression of patients' symptoms <sup>3</sup>.
    - As a side note, the polysaccharide antigen noted above is entirely different from the antigens used in routine vaccinations, which are proteins. **In general, we have not found poor antibody responses to these routine vaccines. In addition, there is no evidence that routine vaccinations cause any detrimental effects on mitochondrial patients. Indeed, the routine vaccinations may play an important role in preventing infections from natural exposure to vaccine organisms.**
- The infection pattern of mitochondrial patients is characteristically similar. The children will have at least one infection per month involving the ears or sinuses. Tubes placement usually does not decrease the number of ear infections <sup>4</sup> These infections, with or without fever, often induce global deterioration. The families frequently report that these patients need to be always on antibiotics because, once the antibiotic are discontinued, they tend to relapse.
- The immunologic evaluation of these patients starts with serum immunoglobulin levels, which are not grossly decreased in most mitochondrial patients, although

occasionally they may have selective IgG subclass deficiency. The most common deficit is found in antibody responses to capsular polysaccharide antigens<sup>3</sup>.

- Pneumococcus, a common polysaccharide-encapsulated organism, has greater than 80 serotypes. Twelve of these serotypes cause most of the respiratory infections in North America. Usually, individuals older than 2 years will respond to at least three serotypes after vaccine challenge. In contrast, mitochondrial patients with recurrent infections respond to less than three<sup>3</sup>.
- The patients' baseline antibody responses to 12 pneumococcal serotypes can be determined by commercially available assays. If they respond to less than three serotypes, patients are given *Pneumovax* (23 valent). Repeat antibody responses are then performed in one month.
- Investigation of mitochondrial patients with recurrent infections and poor antibody response treated with IM gamma globulin replacement shows a dramatic decrease in the number of infections, the number of ER visits, and the number of hospitalizations and school absences<sup>3</sup>.
- It is our opinion that treatment of these patients early with IM gamma globulin will prevent these infectious triggers from promoting mitochondrial deterioration and progression. Questions concerning IM gamma globulin and mitochondrial defects can be directed to [R.Hostoffer@drbobpid.com](mailto:R.Hostoffer@drbobpid.com).

1. Manahan, CL et al, 2004, Chemoattractant signaling in Dictyostelium discoideum, Annual Review of Cell and Dev. Biol. 20, 223-253

2 Disorders of Host Defense, Robert Hostoffer, clinical Management of infections in immunocompromised infants and children, Lippincott Williams&Wilkins, 2001, page 3-32.

3 The Use of Low Dose Intramuscular Immunoglobulin for Prophylaxis against Recurrent Respiratory Tract Infections and Varicella Infections in Children with Mitochondrial Disorders; S. Wallace, R.W.Hostoffer; Journal of Allergy Clin Immunol, vol 117, 2006.

4 Masin, JS, Hostoffer, RW, and Arnold, JE: Otitis media following tympanostomy tube placement in children with IgG<sub>2</sub> deficiency. Laryngoscope. 105: 1188-90, 1995.